

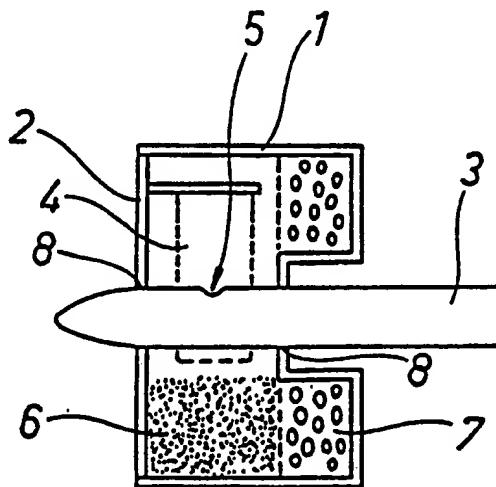


INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : A61M 13/00, 15/00	A1	(11) International Publication Number: WO 92/18188 (43) International Publication Date: 29 October 1992 (29.10.92)
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(21) International Application Number: PCT/FI91/00113 (22) International Filing Date: 15 April 1991 (15.04.91) (71) Applicant (for all designated States except US): HUHTAMÄ-KI OY [FI/FI]; Kärsämäentie 35, SF-20100 Turku (FI). (72) Inventor; and (75) Inventor/Applicant (for US only) : LANKINEN, Tapio [FI/FI]; Jalustinkatu 11, SF-20800 Turku (FI). (74) Agent: LEITZINGER OY; Ruoholahdenkatu 8, SF-00180 Helsinki (FI). (81) Designated States: AT, AT (European patent), AU, BE (European patent), BG, BR, CA, CH, CH (European patent), DE, DE (European patent), DK, DK (European patent), ES, ES (European patent), FI, FR (European patent), GB, GB (European patent), GR (European patent), HU, IT (European patent), JP, KP, KR, LU, LU (European patent), NL, NL (European patent), NO, RO, SE, SE (European patent), SU, US.	Published <i>With international search report. In English translation (filed in Finnish).</i>
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(54) Title: DEVICE INTENDED FOR MEASURING A DOSE OF POWDERED MEDICAMENT FOR INHALATION



(57) Abstract

The invention relates to a device intended for measuring a dose of powdered medicament for inhalation, comprising a medicament container (1), through which extends a shaft (3) provided with at least one dosage recess (5). Container (1) is provided with at least one flap-like sweeper element (4), resting on shaft (3) in alignment with the dosage recess and having one of its ends rotatable around shaft (3), the other end of said flap dragging along the shaft surface, whereafter said shaft (3) is displaceable in its longitudinal direction relative to container (1) so as to bring dosage recess (5), along with a dose of medicament carried therein, outside container (1). The invention relates also to the measuring of a dose of powdered medicament for inhalation by using the device described above.

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Device intended for measuring a dose of powdered medicament for inhalation.

The present invention relates to a section of a powder inhalator required for the inhalation of a powdered medicament, said section containing powdered medicament as well as a mechanism required for measuring its dosage and delivering it out of a reservoir.

The dosage of a medicament for inhalation is generally effected by using a propellant-pressurized dosage aerosol or powder inhalator. With dosage aerosol, the metering of a dose is accurate based on the determination of liquid volume in a dosage valve with external moisture having no effect on the procedure. With powder inhalators, the metering is inaccurate for several reasons. Measuring or metering a dose is based on two prior known principles. The powder may be contained as measured portions in small dosage containers, e.g. capsules, from which it is metered and delivered into the inhalation air of a patient. A larger amount of powdered medicament can also be contained in a reservoir included in an inhalator, wherein a special mechanism is used for delivering a measured amount of powder into the inhalation air of a patient. Such multi-dosage inhalators are more convenient to a patient by virtue of their easy operation.

The medicament doses to be inhaled with powder inhalators may vary within the range of tenths of a milligram to tens of milligrams. The smaller the doses in question, the more difficult it is to effect a sufficiently accurate measuring of the dose and the greater a detrimental effect of extraneous disturbing factors on measuring accuracy. The most significant disturbing factor is external moisture. If a powdered medicament is

moistened, e.g. during storage, it may form lumps for impaired measuring accuracy. The penetrability of moisture into a medicinal substance depends on the tightness of a medicament reservoir, the water-vapour permeability of a structural material as well as on the moisture absorbency of a medicament itself. It is prior known to alleviate the moisture trouble by means of a dehydrating agent associated with a medicament reservoir.

Moisture has also another effect on the accuracy of a medicament dose discharging from an inhalator. If those internal surfaces of an inhalator, which are in contact with discharging medicament powder, become moist, the delivered amount of medicament will be reduced to a fraction of the normal. The moistening may be a result of exhalation through an inhalator or of bringing the device from a cold place to a warm one. This moisture trouble could be inhibited by fitting the inhalator with a one-way valve preventing exhalation and other air-flows occurring through the device.

On the basis of what is stated above, a medicament reservoir and a dose measuring mechanism included in a multi-dosage inhalator should fulfil the following conditions:

- to measure at a sufficient accuracy both large and small doses
- have a structure as tight and compact as possible
- in terms of its structure, to facilitate the use of a one-way valve in the inhalator.

Further, in terms of total medication costs, it would be preferable to use a replaceable medicament reservoir.

Thus, with multi-dosage powder inhalators, the design of a medicament reservoir and a dose measuring mechanism is highly important not only in terms of dose measuring accuracy and stability of a powdered medicament but also a preferred inhalator structure. No prior art multi-dosage powder inhalator is provided with a medicament reservoir and a dose measuring mechanism that would fulfil all the above-mentioned conditions.

Finnish Patent publication No. 69963 discloses a multi-dosage dispenser provided with a medicament container and a dose metering device. The medicament container has a conical lower section and its bottom is provided with a shaft rotatable around its longitudinal axis. The shaft is fitted with one or a plurality of dosage recesses, into which the powder is flowing upon rotating said shaft. The container can be fitted with a dehydrating agent and a vibrator for an intensified flow of the powder upon rotating said shaft. After rotating the shaft through half a turn, the dosage recess has rotated so as to reach an inhalation conduit, which is located below the container and into which the powder drops.

The powdered medicament is well protected against moisture but it is required to have exceptionally good flowing or trickling properties for a uniform filling of the dosage recess. When using a design as described above, it is possible for a patient to receive an overdose of medicament if several loading actions are effected prior to inhalation. The medicament container is not replaceable, nor is there provided a one-way valve for blocking exhalation.

US Patent No. 4 046 146 discloses a multi-dosage inhalator, wherein the dose metering is effected by rotating a cylindrical medicament container having a perforated floor. The cylinder rotates around its centre axis upon a fixed, circular bottom plate provided with a hole for dropping a dose into an inhalation conduit. As the medicament container is rotated, the holes in its floor are filled with a powdered medicament and wind up below a plate inside the container in alignment with a hole in the circular bottom plate, wherethrough the powder falls down gravitationally for inhalation.

The powdered medicament is poorly protected against moisture due to an extensive, untight sliding surface and a hazard of overdoses is ominous if several loading actions are effected prior to inhalation. Measuring of small doses is obviously inaccurate since gravity alone is not sufficient to cause a complete drop of the dose into an inhalation conduit. The design does not allow for effective use of a one-way valve. However, the medicament container is replaceable.

Finnish Patent publication No. 79947 discloses a multi-dosage inhalator, wherein the powder is packed in a medicament reservoir on a perforated sheeting and the perforated point of the sheeting is carried onto an inhalation conduit. In a commercially available device as set forth in this patent, the sheeting comprises a thin, circular plastic disc which, upon effecting a loading action, rotates into an inhalation conduit. The medicament reservoir is provided with a dehydrating agent. Despite the dehydrant, moisture will be able to affect the powdered medicament in time by way of wide and extensive sliding surfaces. The action of this device is troubled by a hazard of blocking the holes of

a perforated plate and the sticking of medicament to the moist interior walls of an inhalation conduit. The medicament reservoir is not replaceable. The mechanism can be used to measure both small and large amounts of medicament.

In the present invention, the question is about a medicament container and a dose measuring mechanism for a multi-dosage powder inhalator for measuring or metering accurately both large and small medicament doses with the powdered medicament permanently and tightly protected from external moisture and for readily facilitating the use of a one-way valve for blocking exhalation through the powder inhalator as well as replaceability.

Operation of the device is based on filling a recess in a cross-sectionally circular shaft with an amount equivalent of a single dose of powdered medicament by rotating a shaft-surrounding medicament container around the shaft and in an inhalation conduit adjacent to the dose by pushing the shaft out of the medicament container. Filling of the recess is effected as a result of the gravity-induced powder rolling and by means of a sweeper element, fastened to the medicament container and leaning against the shaft. The sliding surfaces between shaft and medicament container are elastically tight.

A device of the invention is characterized in that the container is provided with at least one flap-like sweeper element, which rests upon the shaft in alignment with a dosage recess and one of whose ends is rotatable around the shaft, the other end of said flap dragging along the shaft surface, whereafter the shaft is displaceable in its longitudinal direction relative to the

container so as to bring the dosage recess along with a medicament dose contained therein to a position below the container.

The invention will now be described in more detail with reference made to the accompanying drawings, in which

fig. 1 is a basic view of a device of the invention with a medicament container sectioned in the longitudinal direction of the shaft,

figs. 2 a, b and c show the device of fig. 1 in the longitudinal direction of the shaft, wherein the container is turned through a full rotation,

figs. 3 a and b illustrate one embodiment according to the invention,

figs. 4 a and b show an inhalation apparatus including a device of the invention,

fig. 5 illustrates another inhalation apparatus provided with a device of the invention, and

figs. 6 - 9 show one modified embodiment of fig. 5.

Referring to fig. 1, the basic structure of a device is shown with a medicament container sectioned in the longitudinal direction of a shaft 3 and fig. 2 shows it in a cross-section in the direction of the shaft. The device comprises a medicament container housing 1, a gable 2, a circular shaft 3 as well as a sweeper element 4 leaning against the shaft with a slight tension. In alignment with sweeper element 4, said shaft 3 is pro-

vided with a recess 5 for measuring a dose. A powdered medicament 6 lies freely on the floor of medicament container 1. Inside the container it is possible to place a dehydrating agent 7, packed e.g. as an annular body. Shaft apertures 8 are tight but allow for displacement of the shaft in its longitudinal direction. If necessary, there may be a plurality of dosage recesses 5 and those can be located in various parts of shaft 3. The number of sweeper elements 4 can also be more than one. The medicament container 1 has preferably a circular cross-section but other shapes are also possible. The shaft 3 is preferably located centrally in the medicament container but can also be located eccentrically.

A dose measuring or metering procedure is illustrated in figs. 2a, b and c. Upon rotating the medicament container, the powdered medicament first (fig. 2a) rotates along with the container but, upon continued rotation, it starts to trickle and fall downwards ending up on sweeper element 4 (fig. 2b). As one rotation is completed, the sweeper element 4 has packed said dosage recess 5 full of powder with a slight tension (fig. 2c). By pushing shaft 3 the dose can be displaced out of the container and simultaneously the tight shaft aperture 8 trims out a possible excess powder. As a strong gas flow (e.g. induced by inhalation) is directed to dosage recess 5, the latter is exhausted of the powdered medicament. The term "recess" refers to a depression, located in the shaft and having a volume that matches an individual dose of medicament.

Tests have verified that a device provided with a single dosage recess 5 and sweeper element 4 is capable of reaching a measuring accuracy of appr. $\pm 10\%$ when measuring doses of more than 2 mg. In this case, the medicament

container 1 can be half-filled with powder and the measuring accuracy begins to deteriorate after appr. 2/3 of the powder has been spent. Hence, a cylindrical medicament container 1, having a diameter of 2 cm and a height of 1 cm, is capable of measuring or metering more than 200 doses of 2 mg (depending on the specific gravity of a powder in question). Tests have also verified that the flowing characteristics of certain medicinal formulations are insufficient for an accurate operation of the device. This calls for the use of a mechanism which, in a per se known manner, vibrates the medicament container during rotation. The flowing and the filling of a dosage recess can also be intensified by a special design of the interior container wall as well as by adjusting the length and width of a sweeper element and by an eccentric positioning of shaft 5. When measuring doses of less than 2 mg, it is preferable to employ a shaft design as shown in fig. 3, wherein the shaft 3 is hollow at one end slightly beyond said dosage recess 5. Inside the shaft 3 is fitted a stationary tube 9. After dosage recess 5 has been filled, said shaft 3 is pushed out of container 1 while tube 9 retains its position (fig. 3b). As some of the gas flow (e.g. induced by inhalation) is directed to pass through said tube 9, the dosage recess is effectively exhausted of medicament.

The medicament container 1 and the gable with its sweeper element 4 for a device of the invention can be readily manufactured from plastics and the components can be joined together e.g. by press-fitting or ultrasonic welding. If the employed material comprises a suitably elastic material, e.g. soft polyethylene or rather stiff elastomer, no separate shaft sealings 8 are not required. A preferred material for the shaft and its inner tube is

polished stainless steel.

The filling of a medicinal substance in the container can be effected prior to the attachment of a gable to the container, as one of its shaft apertures is closed, or respectively through the other shaft aperture with the gable in position.

A device of the invention can be replaced in the housing of a powder inhalator either without or with a shaft. If a replacement is effected without a shaft, the shaft apertures of a medicament container are protected for the duration of storage by means of a plug, extending through the medicament container and having one of its ends provided with a depression for receiving the shaft end. After removing an empty container from the shaft, the shaft end is placed in this depression and the container is pushed onto the shaft, which forces the plug in front it out of the container. The container will be installed in its proper position according to alignment marks carried therein as well as in the inhalator housing.

A device of the invention is capable of measuring at a sufficient accuracy both very small and large amounts of powder. The powdered medicament is extremely well protected from moisture and its design readily facilitates the use of a one-way valve for blocking exhalation through the device. It is easy to manufacture and its replaceability guarantees reasonable maintenance costs.

The following description deals with examples for assembling a device of the invention to serve as a complete powder inhalator.

Fig. 4a illustrates a simple device, wherein the passage of a dose into an inhalation conduit 10 is effected by manually pressing a button 11. The shaft comprises a massive shaft as shown in fig. 1, one of its ends leaning against a socket 13 tensioned by a spring 12. The medicament container is tensioned in its position by means of an annular, spring-equipped gear mechanism 14, which only allows the rotation of the medicament container in a proper direction and also vibrates the medicament container upon the rotation thereof for a smoother flow of powdered medicament. The shaft is chamfered at 15 in order to maintain its proper position. The example discloses the use of a digital dose counter 16 as well as a contact 17. The container is replaceable by unlocking a clamp unit 18, whereby a section including the container disengages together with its shaft along a line 19 (fig. 4b) and the more expensive section, including the dose counter, is in permanent service.

When using the device, a medicament container 1 is manually turned through one rotation e.g. according to alignment marks, which is followed by pressing in a button 11 and by inhaling through a mouthpiece 20. Upon releasing, the button returns to its original position, whereby the dosage recess pushes itself inside the medicament container is ready for use again.

Fig. 5 illustrates a more complicated embodiment, wherein a device of the invention is used for measuring relatively small amounts of powder in association with a vortex chamber pulverizing pharmaceutical particles, as disclosed in Finnish Patent application 892956. The device employs a shaft design as illustrated in fig. 3. The passage of a dose occurs automatically out of the

medicament container and the inhalator is well protected against moistening caused by exhalation.

The medicament container has a front cover 2, adapted to serve as the rear wall of a vortex chamber 21. The other gable of the container is provided with two meshings, one 22 being in contact with a gear 24 and the other 23 with a spring 25 mounted on the inhalator housing, the purpose of said spring being to prevent rotation of the container in a wrong direction as well as to vibrate the container during rotation. A shaft 26 carries a reversing wheel 27, a splined cylinder 28 as well as a gear 24 and terminates in a prod 29 for supplying an impulse to a digital dose counter 16. A shaft 3 is fitted with a transfer means 30, one of its ends communicating by way of journalled wheels nearly non-frictionally with the slot of splined cylinder 28 as well as with a rail located below the transfer means and in the bottom section of the inhalator.

When reversing wheel 27 is turned through one rotation, said shaft 3 advances into medicament container 1, said inner tube 9 closes the floor of dosage recess 5, the dosage recess fills up, and shaft 3 passes to its original position out of medicament container 1 into said vortex chamber 21. During inhalation through mouth-piece 20, a flap valve 32 serving as a one-way valve opens and air flows through a vortex-chamber inlet tube 33 into the chamber. A small portion of inhalation air travels through dosage recess 5 along tube 9 for thoroughly removing, together with the intra-chamber vortex, the medicament from the dosage recess.

Exhalation through the device can be done through the dosage recess and tube 9. In practice, however, this is

not possible since, when measuring or metering small doses, the hole in the floor of a dosage recess is less than 1 mm in diameter and, thus, a patient does not feel capable of exhaling with a flap valve closing the actual air inlet.

If a massive shaft is employed, exhalation through the device is completely blocked.

The medicament container is replaced by unlocking a hinged portion included in clamp unit 18 and by turning reversing wheel 27 through one rotation. Thus, medicament container 1 comes out as pushed by the shaft, whereby it is easy to pull off of shaft 3. A fresh container is installed in position, as described above (page 9).

Figs. 6 - 9 illustrate one modification to fig. 5 of an inhalation device provided with a novel metering system. In this modification of an inhalation device, a shaft 3 equipped with a dosage recess 5 remains stationary but, instead, a medicament container 1 and its associated vortex chamber 21 along with its nozzle 20 are movable. A separate section including medicament container 1 is disposed around a fixed shaft 3 provided with dosage recess 5, said shaft penetrating through the medicament container. The open end of the medicament container is provided with a vortex chamber 1 along with its nozzle. A portion of medicament container 1 is provided along its outer wall with a projecting stud, fitting in a spiral slot included in the device. When the device is rotated, the stud travelling in the spiral slot of the medicament container forces medicament container 1 along with its vortex chamber outwards, whereby said medicament container 1 moves and rotates

relative to shaft 3. The slot configuration is selected to obtain a complete reciprocating action over a single rotation. In fig. 6, the device is illustrated in a closed inhalation position, wherein the inhalation recess 5 of shaft 3 is located in vortex chamber 21. In fig. 7, the device is illustrated at the half-way point of a loading action, wherein said medicament container 1 has displaced outwards relative to shaft 3 in a manner that said dosage recess 5 is now located in medicament container 1. Fig. 8 shows a cross-section along a line A - A in fig. 6 and fig. 9 illustrates the device in an opened condition for the replacement of a container for a medicinal substance 1.

Claims

1. A device intended for measuring a dose of powdered medicament for inhalation, comprising a medicament container (1), through which extends a shaft (3) provided with at least one dosage recess (5), characterized in that said container (1) is provided with at least one flap-like sweeper element (4), resting on shaft (3) in alignment with the dosage recess and having one of its ends rotatable around said shaft (3), the other end of the flap dragging along the shaft surface, whereafter said shaft (3) is displaceable in its longitudinal direction relative to container (1) so as to bring said dosage recess (5) along with its dose of medicament outside said container (1).
2. A device as set forth in claim 1, characterized in that one of the ends of sweeper element (4) is fastened to the wall of container (1), said container being rotatable around shaft (3).
3. A device as set forth in claim 1 or 2, characterized in that said shaft (3) is at least partially hollow.
4. A device as set forth in claim 3, characterized in that said dosage recess (5) is in communication with the hollow section of shaft (3).
5. A device as set forth in claim 3, characterized in that the wall of shaft (3) is provided with a recess (5) opening into the hollow space and that the hollow space includes a stationary tube (9), which extends into medicament container (1) to the proximity of its other wall past recess (5), said shaft (3) being

pushable relative to the container and said fixed tube (9) through such a distance that said recess (5) is brought outside container (1).

6. A device as set forth in any of the preceding claims, characterized in that said medicament container (1), together with its sweeper element (4) and lead-in sealings (8), is replaceable.

7. A device as set forth in any of the preceding claims, characterized in that the device is provided with a limiter for the direction of container rotation, said limiter preventing the rotation of container (1) in a wrong direction.

8. An inhalation apparatus, provided with a device as set forth in any of the preceding claims intended for measuring a dose of powdered medicament for inhalation.

9. An inhalation apparatus as set forth in claim 8, characterized in that it is provided with a one-way valve (32) for preventing exhalation through the apparatus.

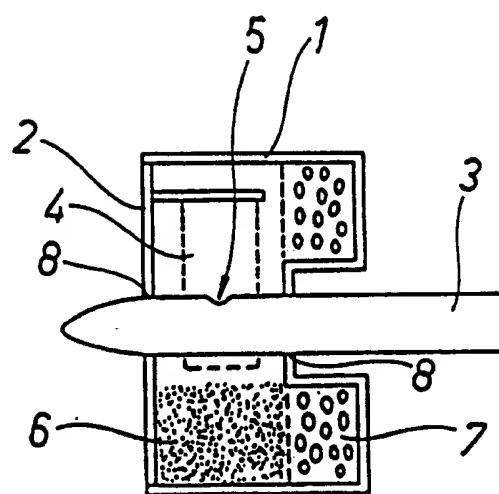


Fig. 1

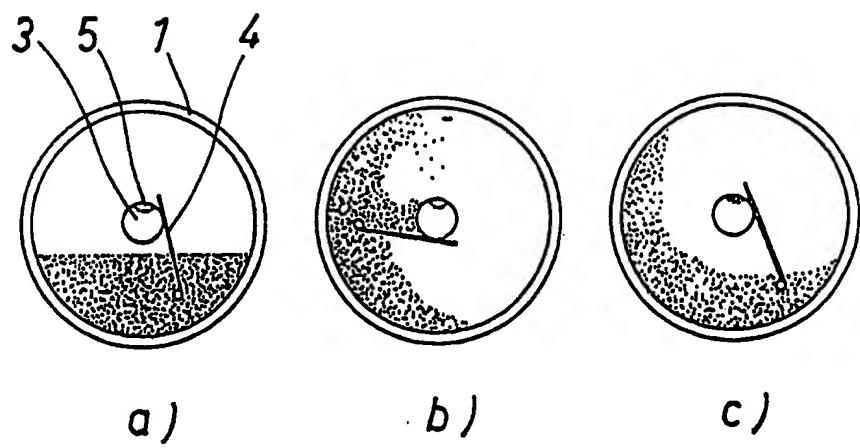


Fig. 2

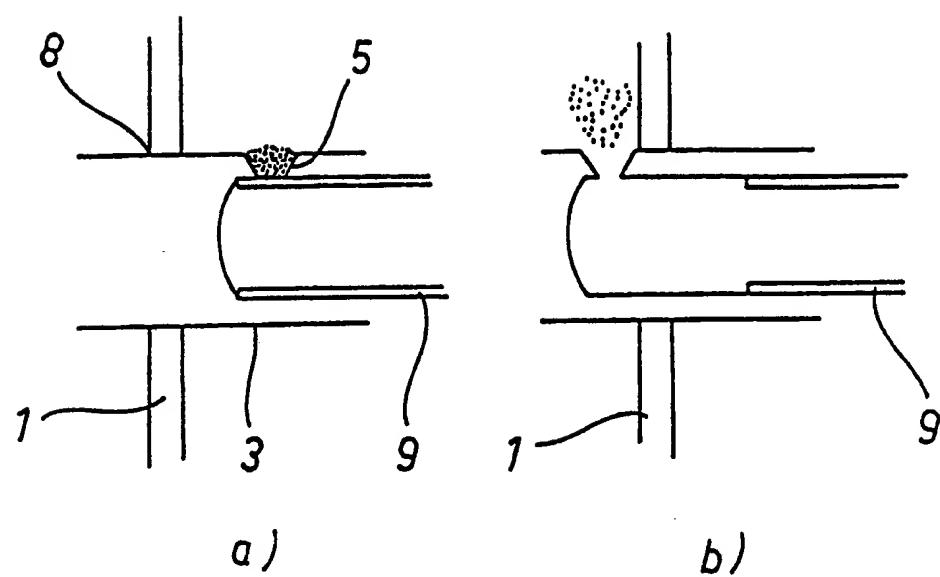


Fig. 3

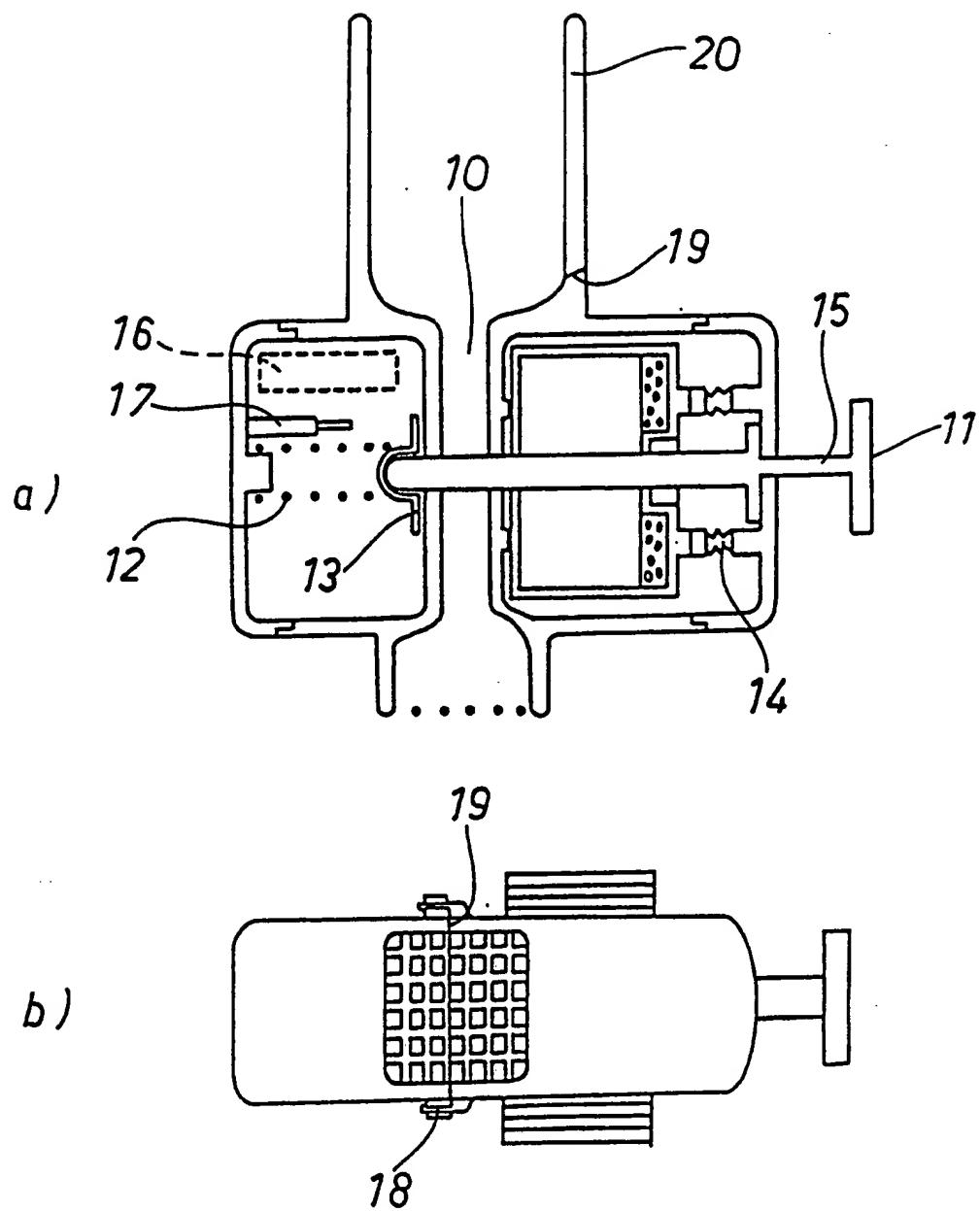


Fig. 4

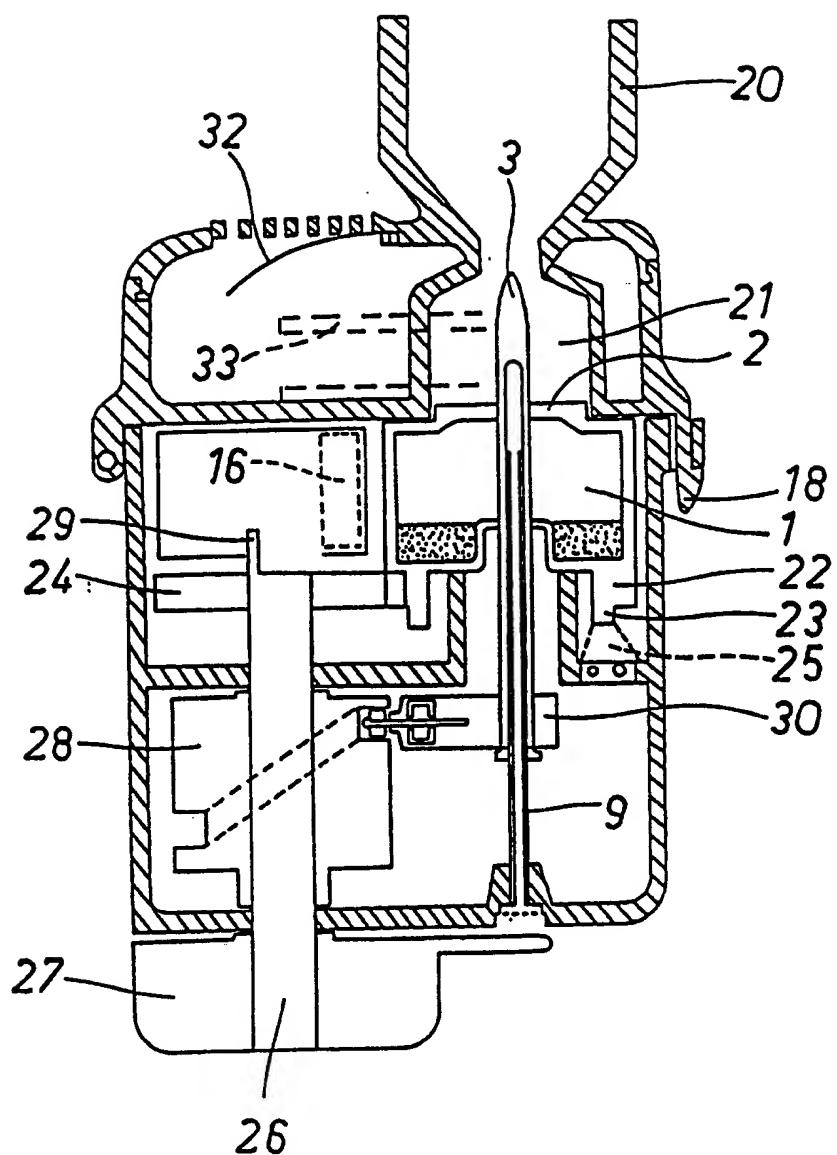
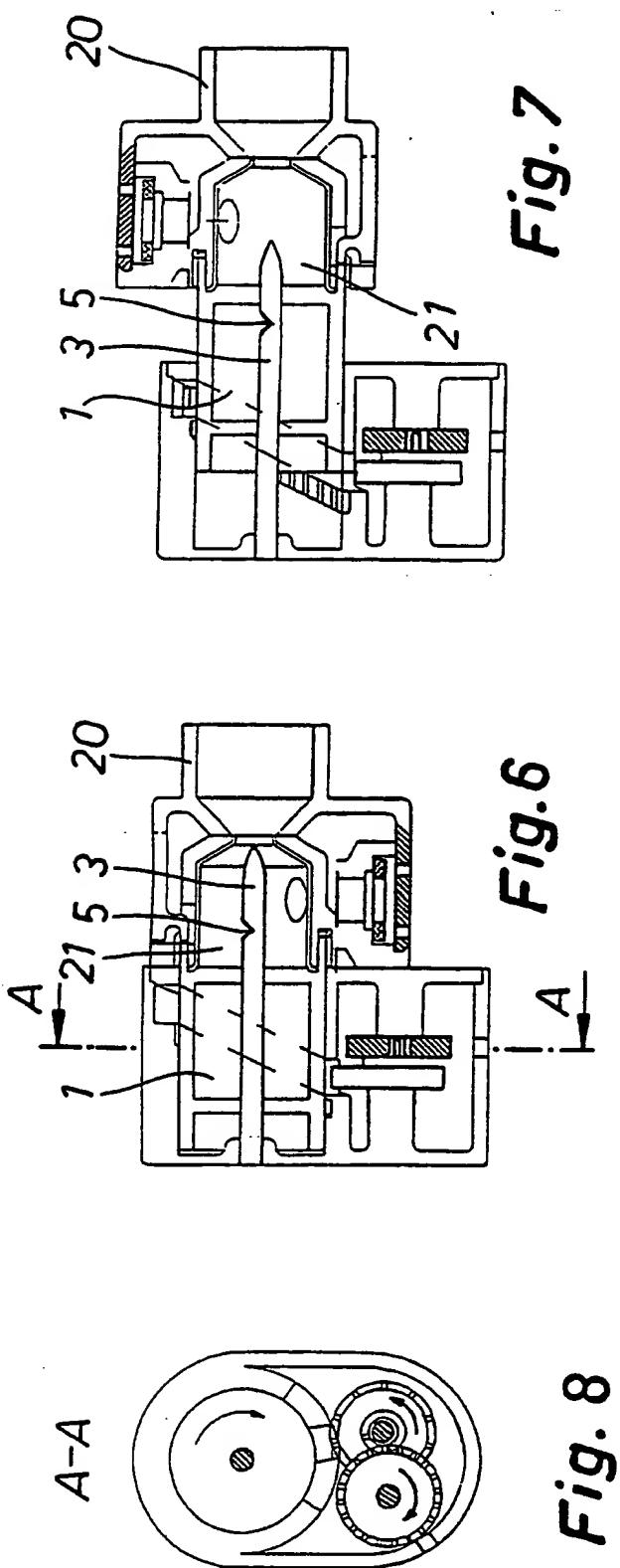


Fig. 5



INTERNATIONAL SEARCH REPORT

International Application No. PCT/FI 91/00113

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all)⁶

According to International Patent Classification (IPC) or to both National Classification and IPC
IPC5: A 61 M 13/00, 15/00

II. FIELDS SEARCHED

Minimum Documentation Searched⁷

Classification System	Classification Symbols
IPC5	A 61 M; G 01 F

Documentation Searched other than Minimum Documentation
to the Extent that such Documents are Included in Fields Searched⁸

SE,DK,FI,NO classes as above

III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹

Category ¹⁰	Citation of Document ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
A	FI, B, 79947 (AKTIEBOLAGET DRACO) 29 December 1989, see the whole document --	1-9
A	GB, A, 2165159 (ORION-YHTYMA OY) 9 April 1986, see the whole document --	1-9
A	Derwent's abstract, No. 90- 73 613/10, SU 1 503 827, publ. week 9010 (GORKI PAEDIATRICS) --	1-9
A	EP, A2, 0407028 (FISONS PLC) 9 January 1991, see the whole document --	1-9

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"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search

25th September 1991

Date of Mailing of this International Search Report

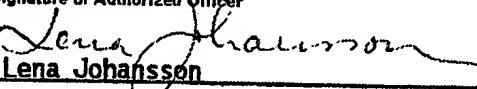
1991-11-18

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Lena Johansson

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
A	US, A, 4046146 (ROSSKAMP ET AL) 6 September 1977, see the whole document -- -----	1-9

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.PCT/FI 91/00113**

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.
The members are as contained in the Swedish Patent Office EDP file on **91-08-30**
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Patent document cited in search report	Publication date	Patent family member(s)		Publication date
FI-B- 79947	89-12-29	NONE		
GB-A- 2165159	86-04-09	CH-A-B-	666823	88-08-31
		DE-A-	3535561	86-05-22
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